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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,408	01/05/2007	Patrick Bosche	BHC 031062	2342

71285 7590 03/30/2010

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EXAMINER	
HOLT, ANDRIAE M	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
03/30/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/576,408	BOSCHE ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3*

10576408 - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 18, 2010 has been entered.

Claims 1-10 are pending in the application. Claim 1 has been amended. Claim 6 is withdrawn as being directed to a non-elected species from the previous Office Action. Claims 1-5 and 7-10 will presently be examined to the extent they read on the elected subject matter of record.

Status of the Claims

Rejections not reiterated from the previous Office Action are hereby withdrawn due to the amendment of the claims. The following rejections are newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Applicant has amended claim 1 to add the limitation "wherein the formulation excludes starch". In light of the fact that starches are carbohydrates, the examiner is interpreting component b) the flavoring agent which is a mixture of proteins, fats, and carbohydrates, as limiting to the flavoring agent to all carbohydrates, except starch.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 and 7-10 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Sherman (US 2003/0229101) in view of Vetter et al. (US 5,808,076) and Lange et al. (US 5,152,986).

Applicant's Invention

Applicant claims a solid pharmaceutical formulation comprising an active pharmaceutical ingredient which is a quinolone antibiotic, 4 to 20% by weight of a flavoring which is a mixture of proteins, fats, and carbohydrates and at least 1.5% to 15% by weight of colloidal silicon dioxide based on the total weight of the finished formulation. Applicant claims the formulation excludes starch. Applicant claims the active pharmaceutical ingredient is enrofloxacin or pradofloxacin.

Determination of the scope of the content of the prior art (MPEP 2141.01)

Sherman teaches tablets that comprise by weight over 80% ciprofloxacin hydrochloride monohydrate, less than 5% starch, and at least 0.5% of a disintegrant selected from crospovidone, croscarmellose sodium, carmellose calcium, and sodium starch glycolate. These compounds are more effective than starch as disintegrants, and hence, can enable adequate disintegration rate with use of a relatively small amount (page 1, paragraph 9). Sherman teaches that the tablets will preferably be free of starch (page 1, paragraph 11). Sherman teaches the tablets will also optionally comprise a glidant. The glidant will preferably be colloidal silicon dioxide. The amount of glidant by weight will preferably be from 0.1% to 2.0% (page 1, paragraph 16) (1.5% - 15%. Sherman teaches that the total of all excipients in the tablets by weight will be under 20% of the tablet weight, so that the tablets will comprise over 80% ciprofloxacin hydrochloride monohydrate by weight. Sherman teaches pharmaceutical tablets are conventionally made by either a wet-granulation process or dry-mix process (page 2, paragraph 17). Sherman teaches that in a wet-granulation process, ingredients are wetted with water or an organic solvent, which will optionally have a binder dissolved therein, and the wet mass is dried and milled into free-flowing granules. The granules are then mixed with other ingredients, and the mixture is then compressed into tablets (page 2, paragraph 18). Sherman further teaches in a dry-mix process will be either a "direct-compression" process or a "dry-granulation" process. In a direct-compression process, the ingredients are mixed together in dry form, and the mixture is then directly

compressed into tablets (page 2, paragraph 19). If, upon dry mixing, the mixture does not flow well enough for direct compression, a procedure known as "dry-granulation", "compaction", or "slugging" may be used. In this process, a mixture of ingredients will first be compacted into relatively large pieces known as "slugs" which are then milled into free flowing granules (page 2, paragraph 20). These granules are then compressed into the final tablets (page 2, paragraph 21). Sherman teaches in example 1, ingredients were mixed in the following proportions, without addition of any solvent: Ciprofloxacin HCl monohydrate 873.0 (quinolone); Crospovidone 18.0; Magnesium stearate 13.5; and Colloidal silicon dioxide 1.5 (colloidal silicon dioxide) (page 2, paragraph 26). Sherman teaches because ciprofloxacin hydrochloride has an unpleasant taste, the tablets will preferably be film-coated to cover the taste (page 2, paragraph 24).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Sherman et al. do not teach the addition of a flavoring agent which is a mixture of proteins, fats, and carbohydrates or that the quinolone is enrofloxacin or pradofloxacin. It is for this reason Vetter et al. and Lange et al. are added as a secondary reference.

Vetter et al. teach that orally administrable formulations of quinolone- or naphthyridonecarboxylic acids can be obtained by mixing quinolone- or naphthyridonecarboxylic acids as such or in the form of their water-soluble salts or derivatives, preferably in the form of their aqueous salt solutions, with embonic (col. 1,

lines 15-26). Vetter et al. teach that the process produces a formulation containing quinolone- or naphthyridonecarboxylic acids which can be administered orally without any problems even to animals which will normally refuse formulations containing quinolone- or naphthyridonecarboxylic acid owing to their bitter taste (col. 1, lines 27-32). Vetter et al. teach preferred compounds are temafloxacin, tosufloxacin, enrofloxacin, and ciprofloxacin (col. 1, lines 62-66). Vetter et al. teach suitable excipients for the formulation are all solid inert substances (col. 2, lines 40-41). Vetter et al. teach examples of organic substances are sugar, food stuff and feed such as milk powder and animal meal (col. 2, lines 44-48) (flavorings). Vetter et al. teach the carrier used may also be a mixture of substances such as colloidal silicas (col. 2, lines 49-58). Vetter et al. teach the formulations prepared according to the invention can be admixed with other excipients, in foodstuff applications these can be for example single feeds or mixtures thereof. Such formulations can be extruded or pelletized in powder form, dry or moist. The formulations can be applied dry on food pellets. The addition of a binder may be useful. Suitable binders are, for example, vegetable, animal or synthetic oils, fats, fatty acids, fatty alcohols, waxes, gelatin, which can also be flavorings (col. 4, lines 66-67- col. 4, lines 1-8).

Lange et al. teach ion exchange resins which are loaded with quinolonecarboxylic acid derivatives, processes for their preparation and their use (col. 1, lines 26-27). Lange et al. teach medicaments, including feed medicaments, which contain ion exchange resins which are loaded with quinolonecarboxylic acid derivatives

of the formula (I). Lange et al. teach preferred active compounds are quinolonecarboxylic acids of the formula (II) include ciprofloxacin and enrofloxacin (col. 3, lines 66-67-col. 1, lines 1-56). Lange et al. teach solid preparations such as powders, premixes or concentrates, granules, pellets, tablets, boli and capsules (col. 5, lines 14-16). Lange et al. further teach for the preparation of solid preparations, the resin loaded with active compound is mixed with suitable excipients, where appropriate with the addition of auxiliaries, and brought into the desired form (col. 5, lines 29-32). Lange et al. teach excipients include organic substances and colloidal silicon dioxide (col. 5, lines 33-39). Lange et al. teach that organic substances are, for example, sugar, cellulose, food-stuffs and feedstuffs such as powdered milk and animal meals (col. 5, lines 40-43). Lange et al. teach the resins loaded with active compound can be mixed with fats and flavorings (col. 6, lines 43-46).

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Sherman, Vetter et al. and Lange et al. and use flavoring agents in the formulation. One of ordinary skill in the art at the time the invention was made would have been motivated to use a flavoring agent in the formulation because it is known in the art as evidence by the teachings of Sherman, Vetter et al. and Lange et al. that quinolone antibiotics have an unpleasant taste. Therefore, the ordinary skilled artisan would have been motivated to use any of the flavoring agents taught by Vetter et al. and Lange et al., including sugar

(carbohydrates), fats, and animal meals, to improve the taste of the quinolone antibiotic taught by Sherman.

One of ordinary skill in the art at the time the invention was made would have been motivated to use enrofloxacin or pradofloxacin as the quinolone antibiotic because it is known in the art that ciprofloxacin, enrofloxacin, and pradofloxacin are from the same class of antibiotics, that have similar modes of action against microbes. In addition, as evidenced by the teachings of Vetter et al. and Lange et al., ciprofloxacin and enrofloxacin are preferred quinolone antibiotics and considered functional equivalents. Therefore, the skilled artisan would have been motivated to substitute one quinolone antibiotic, such enrofloxacin or pradofloxacin, for another, such as ciprofloxacin, because they are functional equivalents.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited reference.

None of the claims are allowed.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is 571-272-9328. The examiner can normally be reached on 9:00 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Andriae M. Holt
Patent Examiner
Art Unit 1616

/John Pak/
Primary Examiner, Art Unit 1616